REMARKS

This communication is responsive to the Office Action mailed March 22, 2005. Claims 1, 2, 4-9 and 19 are allowed. Claims 18 and 20-52 are also pending and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 18 and 20-52 have been rejected under 35 U.S.C. § 112, first paragraph because the examiner states that the specification, while being enabling for a composition comprising SEQ ID NO:6, or for derivatives thereof varying from SEQ ID NO:6 by one amino acid residue, does not reasonable provide enablement for a composition comprising any homologue of the sequence that maintains the biological activities and other characteristics required by claim 18.

Claims 18 and 20-52 have also been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Both the lack of enablement and lack of written description rejections are respectfully traversed and are discussed together below.

Applicants wish to draw the examiner's attention to the fact that the homologous polypeptide as defined in claim 18 must have the physicochemical properties (1) to (6) as recited in claim 18. Such a homologous polypeptide is believed to be easily obtainable for a skilled person according to the guidance provided in the specification and the state of the art at the time this application was filed.

The examiner considers the applicants' arguments are not persuasive, indicating the following two grounds. First, the examiner indicates that there is no demonstration in the art that any homologue of SEQ ID NO:6 that is able to bind an antibody that binds to SEQ ID NO:6 would have the other requisite properties. However, there appears to be a misunderstanding regarding the presently claimed invention. Applicants are not asserting that any homologue of SEQ ID NO:6 that is able to bind an antibody that binds to SEQ ID NO: 6 would have the other requisite properties. Applicants are merely claiming a pharmaceutical composition which comprises a homologue of SEQ ID NO:6, as one embodiment, that has physicochemical properties (1) to (6) as recited in claim 18. Naturally, some homologues which may be detected with a monoclonal antibody which binds to the interferon-gamma inducing polypeptide having an amino acid sequence of SEQ ID NO:6 may not have one or more of the physicochemical

properties (1) to (5) recited in claim 18. However, it should be noted that it is easy for one of skill in the art to test the homologues, which satisfy the physicochemical property (6), with only routine experimentation to see if they also have the physicochemical properties (1) to (5).

For example, the homologous polypeptide as defined by physicochemical property (1) would be easily obtained by one of skill in the art having the wealth of knowledge in the state of the art, such as shown in James D. Watson et al., "*Recombinant DNA*", Second Edition, Scientific American Books, published by W.H. Freeman Company, pp. 191-211, 453-470 (1992), a copy of pertinent disclosures being attached hereto. In particular, page 193 discloses how to obtain site-directed mutants, page 201 discloses that any modification at any position desired in cloned DNA is not only possible, but simple and cheap, and page 466 discloses that it is a routine exercise for protein engineers to generate hundreds of variants of a natural protein for testing. This reference text was published in 1992, well before the effective filing date of this application.

Also attached hereto is a copy of a Declaration executed by Dr. Shizuo AKIRA, which was filed at the European Patent Office during the prosecution of the corresponding

European Patent Application No. 95308055.3 (EP 0712931). In paragraph 25 of the declaration, Dr. AKIRA states as follows:

> It would have been a routine exercise to verify this conclusion by generating variants of SEQ ID NO:1 and screening for the desired inherent biological properties, namely induction of IFN-gamma production by immunocompetent cells, by means of usual recombinant DNA and protein engineering technologies (as illustrated in James D. Watson et al., "*Recombinant DNA*", Second Edition, Chapter 11 and 23, published by W. H. Freeman Company).

The reference cited here in Dr. AKIRA's declaration is the same reference text which is discussed above and attached hereto.

Second, the examiner indicates that applicants do not appear to have provided any examples of interferon gamma inducing polypeptide that bind to such antibodies with the exception of SEQ ID NO:6 itself. However, as explained above, because hundreds mutants of SEQ ID NO:6 can be readily obtained and tested with only routine experimentation by those of skill in the art, applicants believe that disclosure of concrete examples of homologous polypeptides in the specification is not indispensable to providing reasonable enablement for the homologous polypeptides.

With regard to this issue, the examiner states that the teachings of the application in combination with that known in the art as shown by Taniguchi (J. Immunol. Methods

217:9-102) would still be insufficient to establish enablement. However, the examiner's attention is respectfully invited to the fact that the murine homologue of IL-18 was able to induce some interferon gamma production in unmodified human cells, as demonstrated in the Taniguchi reference, setting aside the amount of interferon gamma produced. This means that a homologue as defined in claim 18 does indeed exist.

The examiner further indicates that it is still unclear, even if the teachings as shown in Taniguchi are taken into consideration, which residues had such an effect, and which shared residues may or may not also be open to substitution. However, as discussed above, it would have been easy and routine work for one of skill in the art to produce hundreds of mutants for testing at the time the present application was filed, and furthermore, it would not have been important or critical to know before hand which residues are open to substitution or not. As support, a copy of WO 03/057821 A2, in which some examples of homologous polypeptides as defined in claim 18 are disclosed, is attached hereto. This publication demonstrates that such a homologous polypeptide as defined in claim 18 does actually exist.

In view of the above, the claims comply with 35 U.S.C. § 112 and define patentable subject matter warranting

their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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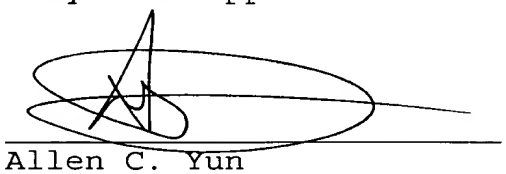
By 
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